# In the
# Supreme Court of the United States.

OCTOBER TERM, 1978.

No. 78-605.

UNITED STATES OF AMERICA, ET AL.,
PETITIONERS,
*v.*
GLEN L. RUTHERFORD, ET AL.,
RESPONDENTS.

ON WRIT OF CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE TENTH CIRCUIT.

## Brief Amicus Curiae of the Commonwealth of Massachusetts and the Massachusetts Department of Public Welfare.

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MISCELLANEOUS.

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### Interest of the Amicus.

Pursuant to Supreme Court Rule 42(4), the Commonwealth of Massachusetts and its Department of Public Welfare, sponsored by the Attorney General of the Commonwealth, submit this amicus curiae brief to support the position of the United States of America that the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act apply to drugs intended for use by the terminally ill.

Like most states,[1] the Commonwealth has enacted legislation which effectively prohibits the in-state sale, distribution or use of any new drug not approved by the Food and Drug Administration (F.D.A.). M.G.L. c. 94C. To the extent that this Court finds the F.D.A.'s restrictions on the use of laetrile by the terminally ill to be constitutionally infirm, the analogous provisions of Massachusetts law are also threatened. Therefore, Massachusetts has a direct interest in protecting its citizens, including the terminally ill, from ineffective and potentially dangerous drugs, and therefore has a direct interest in the outcome of this case.

Massachusetts has also had recent experiences relating specifically to the controversy over laetrile — experiences which would appear to conflict with the assumption made by the Court below that laetrile is non-toxic. The Attorney General represents the Department of Public Welfare in the Chad Green matter in which the parents currently propose to add "metabolic therapy" to court-ordered chemotherapy. *Custody of a Minor*, ____ Mass. ____, 379 N.E. 2d 1053 (1978); *Green* v. *Truman*, 459 F. Supp. 342 (D. Mass. 1978); *Custody of a Minor*, No. 78-6816 (Plymouth, Mass., Superior Court, 1979).

Involvement in this case has given the amicus insights into the laetrile controversy and specifically into the toxicity of the substance which bear directly upon the matters before the Court in the instant case. Therefore, this brief is filed to assist the Court in consideration of the ramifications of the instant case on laetrile-related matters before the states.

[1] Schwartz, "Laetrile: The Battle Moves into the Courtroom," 65 *ABAJ* 224 (1979).



## Questions Presented.

Whether the safety and effectiveness requirements of the Federal Food, Drug and Cosmetic Act apply to drugs intended for use by the terminally ill.

## Statement of the Case.

The Commonwealth of Massachusetts adopts and incorporates herein the statement of the case set forth in the Petitioner's brief.

## Argument.

### Reasons for Deciding in Favor of the United States.

### I. The Medical Affidavit System Created by the Court of Appeals is Unworkable.

The Court of Appeals in *Rutherford* v. *United States*, 582 F. 2d 1234, 1237 (10th Cir. 1978) (*Rutherford VI*), determined that the "safety" and "effectiveness" prerequisites which must be established for new drug approval (21 U.S.C. § 355(d)) do not apply to terminally ill patients.

> We conclude, however, that the permanent injunction granted by the district court should be continued but be limited only to permit procurement of *intravenous injections* administered by a licensed medical practitioner to persons who *are certified by a licensed medical practitioner to be terminally ill of cancer* in some form. *Rutherford VI*, *supra* at 1237 (emphasis added).

The Tenth Circuit assumed "that no applicable or reasonable measure exists" to determine a drug's safety and effectiveness for a terminally-ill patient. *Ibid.* This is an incorrect assumption. A drug's safety and effectiveness for any patient can be determined with regard to a drug's ability to reduce pain, or to counteract symptoms of disease. Nevertheless, assuming *arguendo* that no such measure of effectiveness does exist, then the efficacy of the certification process becomes the primary focus. The immediate question concerns the present ability of medical science to distinguish between a terminal and non-terminal cancer patient. Several expert submissions included in Food and Drug Administration, "Laetrile: Commissioner's Decision on Status," 42 *Fed. Reg.* 39,767 (August 5, 1977), cast severe doubt on the present ability of medical knowledge to make such a distinction. For example,

> Dr. Peter H. Wiernik, Chief of the Clinical Oncology Branch of the National Cancer Research Center, states, "one major difficulty in making a particular chemical available for terminal patients only is that *no one can prospectively define the term 'terminal' with any accuracy.* A patient can be said to be terminal only after he dies. Many patients who are critically ill respond to modern-day management of cancer." (Emphasis added.) Food and Drug Administration, *supra* at 39,805 (August 5, 1977).

Several other cancer researchers echoed Dr. Wiernik's statement.[2]

[2] Note, "Laetrile: Statutory and Constitutional Limitations on the Regulation of Ineffective Drugs," 127 *U. Pa. L. Rev.* 233, 254-255 (1978) (author aptly notes that definitional problem is inherent in nature of cancer, which varies greatly in behavior, rate of growth, symptoms, amount of bodily intrusion, and chances of recovery for patient).



A corollary to this definitional problem is the high probability of intentional abuse of the certification system proposed by the Court of Appeals. In *Custody of a Minor*, No. 78-6816 (Plymouth, Mass. Superior Court, 1979), the child suffers from acute lymphocytic leukemia. His disease is not terminal. *See* George, Aur, Mauer and Simone, "A Reappraisal of the Results of Stopping Therapy in Childhood Leukemia," 300 *N. Eng. J. Med.* 269 (1979). Nonetheless, one of the parent's medical experts testified that he would certify the child under *Rutherford VI* as a terminal cancer patient in order to give him laetrile. This was true even though (1) the child is not terminally ill and (2) the child is receiving laetrile tablets rather than injections. *See also Custody of a Minor*, ____ Mass. ____, 379 N.E. 2d 1053 (1978). It would appear that the prospective conduct of that expert is not aberrational. For example, newspaper reports concerning a Mrs. Pye, who died of acute cyanide poisoning after an accidental overdose of laetrile, reveal that she had a *Rutherford VI* affidavit, even though she was taking laetrile tablets. *The Boston Globe*, February 7, 1979, at 62, Col. 1. Thus, the affidavit system permitted by the court in *Rutherford* is simply unworkable. Given the toxic effects of laetrile and metabolic therapy discussed below, on the one hand, and the problem of definition and intentional abuse on the other, the decision of the Tenth Circuit should be reversed.

## II. The Government Has a Compelling Interest in Protecting the Public from Dangerous Drugs.

This case demonstrates the interaction between the constitutional right to privacy and the duty of government to protect the public from dangerous drugs. The District Court based

its decision on the constitutional right to privacy. The Court of Appeals did not deal directly with this issue:

> We do not reach the constitutional aspects which were applied by the district court. We conclude, however, that the permanent injunction granted by the district court should be continued but be limited only to permit procurement of *intravenous injections* administered by a *licensed medical practitioner* to persons who are certified by a licensed medical practitioner to be terminally ill of cancer in some form. *Rutherford VI, supra*, at 1237 (emphasis added).

The District Court in *Rutherford* v. *United States*, 438 F. Supp. 1287, 1299 (W.D. Okla. 1977) (hereinafter *Rutherford V*), based its decision on the constitutional right of privacy articulated by this Court in such cases as *Roe* v. *Wade*, 410 U.S. 113 (1973), and *Doe* v. *Bolton*, 410 U.S. 179 (1973). In *Rutherford V*, the court, *supra* at 1300-1301, correctly identified the standard which must be met before there may be state interference with the constitutional right of privacy:

> When certain "fundamental rights" are invoked, such as the right of privacy involved herein, regulation may be justified only by a "compelling state interest," and legislative enactments "must be narrowly drawn to express only the legitimate state interests at stake."

The District Court based its conclusion about the constitutional right of privacy on the mistaken assumption that laetrile is not toxic, stating that: "By denying the right to use a *nontoxic substance* in connection with one's own personal health-



care, FDA has offended the constitutional right of privacy." *Id.* at 1301 (emphasis added).

Amicus suggests, however, that laetrile is highly toxic and this alone constitutes a sufficiently compelling state interest for prohibiting selective laetrile use by the terminally ill or anyone else. It is well-accepted that the FDA has a responsibility to protect the public from dangerous drugs being available on the market.

> "There can be no question of the authority of the State in the exercise of its police power to regulate the administration, sale, prescription and use of dangerous and habit-forming drugs . . .. The right to exercise this power is so manifest in the interest of the public health and welfare, that it is unnecessary to enter upon a discussion of it beyond saying that it is too firmly established to be successfully called in question." *Robinson* v. *California*, 370 U.S. 660, 664 (1962), quoting from *Whipple* v. *Martinson*, 256 U.S. 41, 45 (1921).
>
> *See also Whalen* v. *Roe*, 429 U.S. 589, 603, fn. 30 (1977).

The Food, Drug and Cosmetic Act, 21 U.S.C. § 355(a)[3] and (d)(2),[4] provides the necessary authority to keep such "unsafe" drugs off the market. Therefore, if the toxicity of laetrile can be established, the necessary compelling state interest for

[3] "(a) No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug. . . ."

[4] "(d) If the Secretary finds, after due notice to the applicant in accordance with subsection (c) of this section . . ., that . . . (2) the results of such tests show that such drug is unsafe for use under such conditions or do not show that such drug is safe for use under such conditions . . . he shall issue an order refusing to approve the application. . . ."

allowing the FDA to ban laetrile will have been demonstrated. The right of privacy must give way before this compelling state interest.

The evidence currently available demonstrates that laetrile (or more accurately its generic term, amygdalin) contains toxicologically significant amounts of cyanide. *Dorland's Illustrated Medical Dictionary* (24th Ed. 1965) at 73 (definition of amygdalin). In National Academy of Sciences, *Toxicants Occurring Naturally in Foods* (2d Ed. 1973) at 449-450, the toxicity of amygdalin is clearly demonstrated:

> Hydrogen cyanide (HCN) is released by enzymatic hydrolysis of a number of glycosides found in food. Oil of bitter almonds, a generic name for pit oils, including also oils of apricot and peach kernels, contains the glycoside amygdalin. The enzyme emulsin is also present, and when the pits are crushed and moistened, the glycoside is cleaved with the liberation of hydrogen cyanide. . . .
>
> *Toxicologically significant dietary intakes of cyanide result either from improper choice of plant variety,* as with some lima beans, inadequate processing, as may occur with cassava, *or accidental intake, as in the case of a 3-year-old girl who incurred cyanide poisoning from eating approximately 15 apricot kernels containing 0.33% available CN.* (Emphasis added.)

Amydgalin (laetrile) is a cyanogenetic glycoside (cyanide-containing plant) which will yield the deadly poison hydrogen cyanide when the cyanide is cleaved out of the amygdalin. The circumstances when that will happen are as follows:

> Bitter apricot kernels are little "cyanide pellets" because of their millions of subcellulor organelles containing amygdalin and millions of other organelles (lysosomes) containing amygdalin and millions of other organelles (lysosomes) containing B-glucosidase. The cyanide is "safe" as long as the apricot kernel is uncrushed, because it is tightly bound to the benzaldehyde of amygdalin. When an apricot kernel is crushed (by a blender, or the teeth, or anything else) the amygdalin and B-glucosidase make contact and cyanide is generated. The amount of cyanide generated is directly proportional to thoroughness of chewing the kernel. The process of cyanide release from an apricot kernel is analogous to dropping a sodium or potassium cyanide pellet . . . into water or acid, the means of "gas chamber" executions in California and genocidal mass killings by the Hitler regime during World War II. Herbert, "Laetrile: The Cult of Cyanide," 32 *Am. J. Clin. Nut.* (May, 1979) (in press). *See also Toxicants Occurring Naturally in Foods, supra* at 299-306.



A recent laetrile study with dogs confirms this conclusion,[5] and one commentator has noted that ingestion of laetrile itself has led to fatal acute cyanide poisoning:

> A healthy 11-month-old girl accidentally swallowed one to five 500-mg. Laetrile tablets. The pills were labelled "kemdalin — each tab = 500 mgm amigdalin MF,

[5] "The literature contains numerous examples of human poisoning from eating apricot pits . . . since these tissues contain both amygdalin and the enzymes described. However, other plants, e.g., celery, peaches, and bean sprouts, contain B-glucosidases similar to those in almonds . . ..

"Our studies were designed to confirm our prediction that oral laetrile, when ingested with certain uncooked foods containing B-glucosidases, would result in HCN toxicity. In our studies, we were able to reproduce the physiologic and clinical picture of HCN poisoning in dogs after the administration of laetrile and sweet almonds." Schmidt, et al., "Laetrile Toxicity Studies in Dogs," 239 *JAMA* 943 (1978). *See United States* v. *Articles of Food and Drug*, 444 F. Supp. 266 (E.D. Wis. 1977), *aff'd sub nom. United States* v. *Mosinee Research Corp.*, 583 F. 2d 930 (7th Cir. 1978).

. . . (LAETRILE)." The drug belonged to the patient's father, who was using it for the treatment of a cancer and considered the pills to be harmless vitamins . . ..

In view of the hospital course and autopsy findings consistent with cyanide poisoning by the oral route, the cyanide demonstrated in blood and urine, and the negative studies for other possible toxins, we conclude that our patient died of subacute cyanide poisoning secondary to the accidental ingestion of amygdalin tablets. Braico, et al., "Laetrile Intoxication; Report of a Fatal Case," 300 *N. Eng. J. Med.* 238, 240 (1979).

*See also, The Boston Globe,* February 7, 1979, at 62, Col. 1 (article reporting December 3, 1978, death of 42-year-old California woman as a result of overdose of laetrile tablets).

Laetrile proponents admit that laetrile by itself is worthless but argue that laetrile must be used in conjunction with so-called metabolic therapy. Manner, *The Death of Cancer* (1978); Halstead, *Amygdalin (Laetrile) Therapy* (1977). However, the principal components of so-called "metabolic" therapy are themselves toxic in the dosages prescribed. They include a daily enema composed of proteolytic enzymes. These may destroy tissue in the colon. Goodman, L., and Gilman, A., *The Pharmacological Basis of Therapeutics* (5th Ed. 1975) at 958. Another component consists of megadoses of Vitamin A far above the recommended daily allowances. Vitamin A is fat soluble and will build up in the liver and cause hypervitaminosis A. *See* Goodman and Gilman, *supra* at 1574, and National Academy of Sciences, *Recommended Daily Allowances* (8th Ed. 1974) at 152. Another component is megadoses of Vitamin C which may affect fetal development. Herbert, "The Rationale of Massive-Dose Vitamin Therapy (Mega Vitamins Therapy: Hot Fictions vs. Cold Facts)," in P. White and N. Selvey, *IV Proceedings: Western Hemisphere Nutrition*



*Congress* 84, 87 (1975). It is indisputable that cyanide toxicity can cause acute poisoning leading to death (as at Jonestown). Smaller intakes of cyanide lead to chronic cyanide poisoning. In *Custody of a Minor,* No. 78-6816 (Plymouth, Mass., Superior Court, 1979), the child was shown to be suffering from chronic cyanide poisoning as a direct result of his daily intake of one 500-mg. laetrile tablet. There was expert testimony that the child had a cyanide level in his blood which was comparable to that of a heavy adult smoker. That this level of cyanide will culminate in progressive deafness and blindness by poisoning from laetrile is well-documented in the literature.

Chronic cyanide intoxication from laetrile in the diet has produced in Africa thousands of cases of slowly progressing neurologic damage with blindness (bilateral optic atrophy), nerve deafness, and myelopathy, with muscle weakness in a demyelinating syndrome of toxic ataxic neuropathy and variants of it. Herbert, "Laetrile: The Cult of Cyanide," *supra*; *see also Toxicants Occurring Naturally in Foods, supra* at 305; B.O. Osuntokun, "Cassava diet and cyanide metabolism in Wistar rats," 24 *Br. J. Nutr.* 797 (1970); "Chronic Cyanide Neurotoxicity," ii *Lancet* 942 (1969). *See generally* United States Senate, Subcommittee on Health and Scientific Research, Committee on Human Resources, 95th Cong., 1st Sess., *Banning of the Drug Laetrile from Interstate Commerce by FDA* (Comm. Print 1977).

## III. The Constitutional Right of Privacy Must Give Way Before the Compelling Need to Protect the Public from Laetrile Toxicity.

The constitutional right of privacy applies to the relationship of physician and patient. *Loe* v. *Bolton,* 410 U.S. 179

(1973). *But see Fitzgerald* v. *Porter Memorial Hospital*, 523 F. 2d 716 (7th Cir. 1975), *cert. den.* 425 U.S. 916 (1976). However, at the same time, "the State has broad police powers in regulating the administration of drugs by the health professions." *Whalen* v. *Roe*, 429 U.S. 589, 603, fn. 30 (1977). *See also Carey* v. *Population Services International*, 431 U.S. 678 (1977), and *Smith* v. *Organization of Foster Families for Equality & Reform*, 431 U.S. 816 (1977).

In regard to laetrile, some courts have found the privacy interest to be paramount. For example, a California intermediate appellate court has held that:

> This state protected right of privacy encompasses a fundamental and compelling interest of the cancer patient to choose or reject his or her own medical treatment on the advice of a licensed medical doctor. This right can be abridged only where there is compelling need. *People* v. *Privitera*, 74 Cal. App. 3d 936, 141 Cal. Rptr. 764, 777 (1977). (The case is awaiting decision by the California Supreme Court and thus the decision of the intermediate appellate court has no precedential value.)

The *Privitera* court found that the state had not established the compelling need necessary to abridge the right of privacy.

However, "The Legislature has the right to control distribution and use of drugs which are narcotic, habit forming, hallucinatory or toxic . . . but to limit its power to just these kinds of drugs portends a frightening parade of horribles. Protection of public health, safety and welfare demands more." *People* v. *Privitera*, *supra*, 141 Cal. Rptr. at 787 (Cologne, J., dissenting). The purpose of the Food, Drug and Cosmetic Act and of similar state statutes is to protect the public from unproven, unsafe or ineffective drugs. 21 U.S.C. § 351; *United*



*States* v. *Bel-Mar Laboratories, Inc.*, 284 F. Supp. 875 (E.D. N.Y. 1968). Laetrile has been shown to be toxic because of the presence of cyanide. *See* Sadoff, Fuchs and Hollander, "Rapid Death Associated with Laetrile Ingestion," 239 *JAMA* 1532 (1978); and Townsend and Boni, "Cyanide Poisoning From Ingestion of Apricot Kernels," 24 *Morbid Mortal* 427 (1975). "Amygdalin [laetrile] is not generally recognized by experts qualified by scientific training and experience to evaluate its safety, as having been shown through scientific procedures . . . to be safe under the conditions of its use." *United States* v. *General Research Laboratories*, 397 F. Supp. 197, 199 (C.D. Cal. 1975). The District Court in *United States* v. *Articles of Food and Drug*, *supra*, found that,

> 1. "Amygdalin is a cyanogenic glucoside [*sic*] which reacts with Beta-glucosidase, an enzyme found in a number of commonly eaten foods, to form hydrogen cyanide, a highly toxic substance." *Id.* at 271.
> 2. "Due to the presence therein of cyanide, a poisonous and deleterious substance, amygdalin is potentially harmful and ordinarily injurious to health." *Ibid.*
> 3. "The promotion or sale of amygdalin for any food or drug use constitutes a fraud on the consuming public." *Id.* at 273.[6]

Therefore, the FDA should be upheld in its efforts to eliminate laetrile from the marketplace.

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[6] There is less indication of toxicity of injected laetrile since the cyanide is not liberated by Beta-glucosidase and probably passes through the body whole. Herbert, "Laetrile: The Cult of Cyanide," *supra*, at ____ (in press); on the other hand, there is no reliable evidence that injected laetrile has antineoplastic capabilities. Stock, et al., "Antitumor Tests of Amygdalin in Spontaneous Animal Tumors," 10 *J. Oncology* 89 (1978).

Finally, there is a second aspect to the compelling interest argument. The carving out of an exception to the Food, Drug and Cosmetic Act for the terminal patient may either lead a non-terminal patient to forgo effective treatment or cause a patient currently undergoing effective treatment to shift to unproven treatments. *See Custody of a Minor, supra*; *In re Hofbauer*, 411 N.Y.S. 2d 416 (App. Div. 1978). These problems are very real because of the relative ease with which any patient can acquire a "*Rutherford* affidavit." The results can only be needless suffering for those persons who mistakenly decline beneficial treatment because of the lure of unsafe remedies.

**Conclusion.**

For the reasons articulated in the argument, the decision of the Court of Appeals should be reversed.

Respectfully submitted,

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